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Guideline No. 426: Hypertensive Disorders of Pregnancy: Diagnosis, Prediction, Prevention, and Management

(En français : Directive clinique n° 426 : Troubles hypertensifs de la grossesse : Diagnostic, prédiction, prévention et prise en charge)

The English document is the original version. In the event of any discrepancy between the English and French content, the English version prevails.

This clinical practice guideline was prepared by the authors and overseen by the SOGC's Maternal Fetal Medicine Committee. It was reviewed by the SOGC Clinical Practice – Obstetrics Committee and approved by the SOGC Guideline Management and Oversight Committee and the SOGC Board of Directors. This clinical practice guideline supersedes No. 307, published in May 2014.

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This document reflects emerging clinical and scientific advances as of the publication date and is subject to change. The information is not meant to dictate an exclusive course of treatment or procedure. Institutions are free to amend the recommendations. The SOGC suggests, however, that they adequately document any such amendments.

Informed consent: Patients have the right and responsibility to make informed decisions about their care in partnership with their health care provider. In order to facilitate informed choice, patients should be provided with information and support that is evidence-based, culturally appropriate, and personalized. The values, beliefs and individual needs of each patient in the context of their personal circumstances should be considered and the final decision about care and treatment options chosen by the patient should be respected.

Language and inclusivity: The SOGC recognizes the importance to be fully inclusive and when context is appropriate, gender-neutral language will be used. In other circumstances, we continue to use gendered language because of our mission to advance women's health. The SOGC recognizes and respects the rights of all people for whom the information in this document may apply, including but not limited to transgender, non-binary, and intersex people. The SOGC encourages health care providers to engage in respectful conversation with their patients about their gender identity and preferred gender pronouns and to apply these guidelines in a way that is sensitive to each person's needs.

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Weeks' Gestation Notation: The authors follow the World Health Organization's notation on gestational age: the first day of the last menstrual period is day 0 (of week 0); therefore, days 0 to 6 correspond to completed week 0, days 7 to 13 correspond to completed week 1, etc.

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RECOMMENDED CHANGES IN PRACTICE

1. Do not screen low-risk normotensive women for proteinuria.
2. Implement home blood pressure monitoring for hypertensive outpatients to rule-out white-coat effect.
3. Among women with chronic hypertension, do not diagnose superimposed preeclampsia based solely on a rise in BP.
4. To assess women with suspected preeclampsia, use angiogenic markers (such as soluble fms-like tyrosine kinase-1 [sFlt-1] and/or placental growth factor [PlGF]), where available.
5. Formalize the risk of adverse maternal outcomes among hypertensive women by using predictive models.
6. To predict preeclampsia in early pregnancy, use clinical risk markers, along with blood pressure, uterine artery pulsatility index, and biochemical markers, where available.
7. Consider obesity a high-risk factor for preeclampsia, warranting preventive therapy with acetylsalicylic acid.
8. Encourage all women to exercise in pregnancy to prevent preeclampsia.
9. Consider using doses of acetylsalicylic acid higher than 81 mg/d in all women at increased risk of preeclampsia.
10. For safe transport, optimize maternal and fetal conditions.
11. Treat hypertension in pregnancy, from a threshold of 140/90 mm Hg and to a target diastolic BP of 85 mm Hg.
12. Consider timed birth in women with preeclampsia from 36^0 weeks.

KEY MESSAGES

1. The hypertensive disorders of pregnancy remain an important cause of maternal and perinatal mortality and morbidity, requiring surveillance to detect rapid deterioration and comprehensive treatment.
2. Preterm preeclampsia can be largely prevented with low-dose acetylsalicylic acid started before 16 weeks gestation.
3. Hypertensive disorders of pregnancy, particularly preeclampsia, are associated with an increased risk of long-term maternal hypertension and cardiovascular disease.

ABSTRACT

Objective: This guideline was developed by maternity care providers from obstetrics and internal medicine. It reviews the diagnosis, evaluation, and management of the hypertensive disorders of pregnancy (HDPs), the prediction and prevention of preeclampsia, and the postpartum care of women with a previous HDP.

Target population: Pregnant women.

Benefits, harms, and costs: Implementation of the recommendations in these guidelines may reduce the incidence of the HDPs, particularly preeclampsia, and associated adverse outcomes.

Evidence: A comprehensive literature review was updated to December 2020, following the same methods as for previous Society of Obstetricians and Gynaecologists of Canada (SOGC) HDP guidelines, and references were restricted to English or French. To support recommendations for therapies, we prioritized randomized controlled trials and systematic reviews (if available), and evaluated substantive clinical outcomes for mothers and babies.

Validation methods: The authors agreed on the content and recommendations through consensus and responded to peer review by the SOGC Maternal Fetal Medicine Committee. The authors rated the quality of evidence and strength of recommendations using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, along with the option of designating a recommendation as a "good practice point." See online Appendix A (Tables A1 for definitions and A2 for interpretations of strong and conditional [weak] recommendations).The Board of the SOGC approved the final draft for publication.

Intended users: All health care providers (obstetricians, family doctors, midwives, nurses, and anesthesiologists) who provide care to women before, during, or after pregnancy.

RECOMMENDATIONS:

1. Pre-conception counselling is suggested for women with pre-pregnancy hypertension to advise on individualized management during pregnancy (*conditional, low*).
2. Replacing angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) with other antihypertensives in women planning pregnancy is recommended unless there is a compelling clinical indication not to (*strong, low*).
3. In early pregnancy, women should be screened, at a minimum, for clinical risk markers for preeclampsia (*strong, moderate*).
4. If testing is available, women should be screened at 11−14 weeks gestation using a combination of clinical risk markers, uterine artery pulsatility index, and placental growth factor (PlGF) to individualize the risk of developing preeclampsia (*strong, moderate*).

5. For women at increased risk of preeclampsia, low-dose acetylsalicylic acid (81 or 162 mg/d) is recommended (*strong, high*), to be taken at bedtime (*strong, moderate*), preferably before 16 weeks gestation (*conditional, moderate*), and discontinued by 36 weeks gestation (*conditional, low*).
6. For all other women, low-dose acetylsalicylic acid is not recommended (*strong, moderate*).
7. For all women with low dietary intake of calcium ($<$900 mg/d), oral calcium supplementation of at least 500 mg/d is suggested to prevent preeclampsia (*conditional, low*).
8. For all women, vitamin D supplementation over and above Health Canada's recommendation for adults is not suggested to prevent preeclampsia (*conditional, moderate*).
9. For all women, exercise is recommended to prevent preeclampsia (*strong, moderate*).
10. For women at increased risk of preeclampsia, who are overweight or obese dietary advice (reduce calories and choose foods with a low glycemic index) and exercise are recommended (*conditional, moderate*).
11. Inpatient care should be provided for women with severe hypertension or preeclampsia with 1 or more maternal adverse conditions (*good practice point*).
12. Bed rest is not suggested for any women with preeclampsia (*conditional, low*).
13. Antihypertensive therapy is recommended for pregnant women with an average systolic blood pressure $\geq$140 mm Hg or diastolic blood pressure $\geq$90 mm Hg, regardless of the hypertensive disorder of pregnancy (*strong, moderate*).
14. A diastolic blood pressure of 85 mm Hg should be targeted for pregnant women on antihypertensive therapy with chronic or gestational hypertension (strong, moderate), and a similar target, considered for women with preeclampsia (*conditional, low*).
15. Antihypertensive therapy (oral or parenteral) is urgently recommended for women with severe hypertension (i.e., systolic blood pressure $\geq$160 mm Hg or diastolic blood pressure $\geq$110 mm Hg) in pregnancy or postpartum (*strong, low*).
16. Magnesium sulphate is recommended for first-line treatment of eclampsia and prophylaxis against eclampsia in women with preeclampsia and severe hypertension or adverse maternal conditions (*strong, high*).
17. Platelet transfusion should be considered if a woman's platelet count is $<20 \times 10^9$/L before vaginal delivery or $<50 \times 10^9$/L before cesarean delivery, or at any time if there is excessive active bleeding, known platelet dysfunction, rapidly falling platelet count, or coagulopathy (*strong, low*).
18. For women with chronic hypertension, expectant care should be undertaken from fetal viability to $<37^0$ weeks gestation, unless there is an indication for birth (*strong, very low*). Initiation of delivery can be offered at 38^0 to 39^6 weeks gestation but should be advised from 40^0 weeks gestation *(conditional, low*).
19. For women with gestational hypertension, expectant care should be undertaken from fetal viability to $<37^0$ weeks, unless there is an indication for birth (*strong, low*). When gestational hypertension arises before 37^0 weeks, initiation of delivery can be offered at 38^0 to 39^6 weeks gestation but should be advised from 40^0 weeks gestation (*conditional, low*). For women who are already at 37^0 weeks gestation or later and present with gestational hypertension, initiation of delivery should be discussed (*strong, moderate*).
20. For women with preeclampsia, expectant management may be considered from fetal viability until $<34^0$ weeks gestation, but only in perinatal centres capable of caring for very preterm infants (*conditional, moderate*). At 34^0–35^6 weeks gestation, initiation of delivery should be discussed, as it decreases maternal but increases neonatal risk, particularly if antenatal corticosteroids are not prescribed (*strong, moderate*). At 36^0–36^6 weeks gestation, initiation of delivery should be considered (*strong, moderate*). At 37^0 weeks gestation or later, initiation of delivery is recommended (*strong, high*).
21. Blood pressure should be measured regularly (at least twice) in the first 2 weeks after delivery in women with hypertension (*good practice point*).
22. As women may develop preeclampsia for the first time postpartum, those with new or worsening hypertension and/or symptoms of preeclampsia should be evaluated accordingly (*good practice point*).
23. For lactating women, the following antihypertensive drugs are suggested: labetalol, methyldopa, nifedipine, enalapril, and captopril (*conditional, low*).
24. Clinical follow-up should be provided for women with gestational hypertension and preeclampsia to ensure normalization of hypertension, clinical features, and laboratory test results (*good practice point*).
25. Women with gestational hypertension and preeclampsia may benefit from interventions to reduce their risk of a hypertensive disorder of pregnancy in a future pregnancy and from screening for cardiovascular risk factors (*conditional, low*).

INTRODUCTION

Hypertensive disorders of pregnancy (HDPs) are a leading cause of maternal and perinatal mortality and morbidity. As a consequence, antenatal care is devoted in large part to their detection.

The purpose of this guideline is to support evidence-based care of women who are

- planning a pregnancy and are at risk of an HDP;
- pregnant and either at risk of an HDP or have elevated blood pressure (BP); or
- postpartum and had an HDP in the past.

Our health intent and aim is to improve maternal and perinatal outcomes by promoting evidence-based practice to reduce the incidence of preeclampsia and optimize management of all HDPs. The target users are multidisciplinary maternity care providers at all levels of health care.

This guideline updates the 2014 version and responds to user feedback that the guideline should be more succinct. We have reduced the number of recommendations, from 154 to 25, by focusing on key aspects of practice and removing sections on obstetric anesthesia, pediatric follow-up, the patient perspective, and knowledge translation and tools. We have increased our use of tables and figures, integrated HDP definitions and associated investigations into a new table, included new information about the secondary causes of chronic hypertension, combined our prevention recommendations for women at increased risk and at low risk, and provided a transport checklist for women with preeclampsia who are moved to referral centres. The text complements, but does not duplicate, information provided in the tables and figures. We have also ensured harmonization of our recommendations with other Society of Obstetricians and Gynaecologists of Canada (SOGC) guidleines and other relevant national guidelines, including those from Hypertension Canada.

ABBREVIATIONS

ACE	angiotensin-converting enzyme
ACR	albumin:creatinine ratio
ARB	angiotensin-receptor blocker
ASA	acetylsalicylic acid
AST	aspartate aminotransferase
ALT	alanine aminotransferase
CKD	chronic kidney disease
FHR	fetal heart rate
FMF	Fetal Medicine Foundation
HDP	hypertensive disorder of pregnancy
PCR	protein:creatinine ratio
PIERS	Pre-eclampsia Integrated Estimate of Risk Score
PIGF	placental growth factor

DIAGNOSIS, CLASSIFICATION, AND INVESTIGATIONS

Tables 1 and 2 define hypertension and proteinuria in pregnancy, as well as the classification of the hypertensive disorders of pregnancy.

Blood Pressure Measurement

A diagnosis of hypertension should not be based on a single BP reading. We recommend averaging BP measurements, acknowledging that BP tends to fall during a medical visit, and that taking only the second or last measurement is not a valid reflection of the actual BP. Ideally, BP should be measured serially with an automated device until it is stable (i.e., until consecutive readings are within 10 mm Hg systolic and 6 mm Hg diastolic) in both arms, particularly if there is hypertension, and then the last 2 measurements for the visit should be averaged.[1] If BP is severely elevated, measurements should be repeated within 15 minutes at most, while antihypertensive therapy can be readied if needed.

In pregnancy, BP should be measured using a standardized technique and either a calibrated aneroid device or an automated device validated for use in pregnancy and preeclampsia.[2] This advice applies to all settings, including clinics, day units, antenatal home care programs, and self-measurement at home (see below). The BUMP 1 trial, currently underway, will clarify whether self-monitoring of BP at home leads to earlier diagnosis of hypertension and improves outcomes.[3]

Once BP is found to be elevated in an "office" setting, using a validated device, "out-of-office" BP monitoring is advised to confirm the diagnosis of hypertension and assess whether there is an element of white-coat hypertension (Box 1). Observational data suggest that self-monitoring of BP among women with hypertension may reduce interventions (such as labour induction) and health care utilization;[4] whether clinical outcomes are improved will be clarified by the BUMP 2 trial.[3]

The definition of hypertension in pregnancy continues to be based on a diagnostic threshold of 140/90 mm Hg when measured in the office/clinic setting. The authors recognize that the American Heart Association and American College of Cardiology define hypertension from a threshold of

Table 1. The hypertensive disorders of pregnancy, investigations and monitoring, graded according to the quality of evidence

	Definition	Investigations/monitoring
Hypertension	Hypertension is an office (or in-hospital) systolic BP ≥140 mm Hg and/or diastolic BP ≥90 mm Hg, based on the average of at least 2 measurements, taken after 5 minutes' rest, at least 15 minutes apart, using the same arm (high)	• When <160/110 mm Hg, hypertension should be confirmed by out-of-office monitoring using a device validated for use in pregnancy and preeclampsia if at all possible (*strong*) • A home BP ≥135/85 mm Hg confirms the diagnosis of hypertension (*moderate*) • Frequency and nature of follow-up depends on the hypertensive disorder (see below) (*GPP*)
Severe	Systolic BP ≥160 mm Hg and/or a diastolic BP ≥110 mm Hg based on the average of at least 2 measurements, taken within 15 minutes at most, using the same arm (*high*)	• Women should be evaluated and treated with antihypertensive therapy in hospital (*high*) • Continuous fetal heart rate monitoring is advised until BP is stable (low)
Transient	Elevated BP, typically in the office setting (≥140/90 mm Hg), that resolves with repeated BP measurement (high)	More frequent BP measurement is warranted based on an elevated risk of preeclampsia or sustained hypertension (*GPP*)
White-coat	An office BP ≥140/90 mm Hg, but an out-of-office BP <135/85 mm Hg (*high*)	More frequent BP measurement is warranted based on an elevated risk of preeclampsia (*moderate*)
Masked	An office BP <140/90 mm Hg, but an out-of-office BP ≥135/85 mm Hg (*high*)	Follow-up is guided by the complications that prompted out-of-office BP monitoring in the woman (GPP)
Proteinuria	Proteinuria is defined as ≥30 mg/mmol urinary PCR in a spot (random) urine sample, or ACR ≥8 mg/mmol,[133] or ≥0.3 g/day in a complete 24-hour urine collection (*high*)	• Proteinuria screening for preeclampsia risk in low-risk normotensive women is not recommended[18] (*low*) • More definitive testing for proteinuria (by urinary PCR, ACR, or 24-hour urine collection) should be performed when preeclampsia is suspected, including ≥1 dipstick result for proteinuria in women with hypertension and rising blood pressure and in women with normal blood pressure, but symptoms or signs suggestive of preeclampsia (*moderate*) • Proteinuria testing does not need to be repeated once proteinuria criteria for preeclampsia have been met (*moderate*)
Chronic (pre-existing) hypertension	Hypertension that develops either before pregnancy or at $<20^0$ weeks (*high*)	• Consider investigations for target organ damage and secondary causes of hypertension, as clinically indicated (Table 4) (*GPP*) • Frequency of follow-up should be guided by BP level and other individual risks of adverse outcome (*GPP*)

ACR: albumin:creatinine ratio; ALT: alanine aminotransferase; AST: aspartate aminotransferase; BP: blood pressures; GPP: good practice point; PCR: protein:creatinine ratio.

130/80 mm Hg (i.e., stage 1 hypertension as 130–139/80–89 mm Hg and stage 2 as ≥140/90 mm Hg), but Hypertension Canada has not adopted this lower threshold.[5] Also, while women with stage 1 hypertension have an increased risk of adverse pregnancy outcomes,[6] the clinical and cost-effectiveness of implementing a lower diagnostic threshold for hypertension have not yet been studied.

Out-of-office BP monitoring is most commonly undertaken at home. Available lists of automated devices validated for use in pregnancy and preeclampsia are not specific to Canada.[2,7] Care providers should explore which devices are available locally, encourage women to purchase them, and advise women to bring their monitor to all antenatal care appointments so that the device can be checked against a calibrated office BP device. A standardized approach to doing so is available.[8]

BP measured out-of-office is generally lower than that measured in office among hypertensive women, leading to the diagnostic criteria for hypertension outlined in Table 1; there is, however, wide variation.[9] (Use of out-of-office BP values to guide antihypertensive therapy is discussed in the section on antihypertensive therapy.)

Table 2. Definitions of the hypertensive disorders of pregnancy, maternal and feto placental surveillance, graded according to the quality of evidence

	Definition	Maternal surveillance	Feto-placental surveillance

Gestational hypertension	Hypertension that develops for the first time at $\geq 20^0$ weeks, without evidence of preeclampsia (Table 4) (*high*)	Diagnosis:
		Women should undergo testing for preeclampsia to rule it out (*high*)
		Follow-up:
		Proteinuria testing should be performed at each subsequent antenatal visit (*moderate*)
		If preeclampsia is suspected on clinical grounds, the woman should be re-evaluated for preeclampsia (*high*)
		The risk of adverse maternal outcomes increases with earlier gestational age and/or the onset or worsening of the following (women should be informed to report these between visits) (*high*):
		• symptoms
		  ◦ headache/visual disturbances
		  ◦ chest pain/dyspnea
		  ◦ vaginal bleeding with abdominal pain
		• systolic blood pressure (if self-monitoring)
		• dipstick proteinuria (if self-monitoring)
		• pulse oximetry (if self-monitoring)
			Diagnosis:
			• Angiogenic markers (if available) could be performed; if normal,[c] the diagnosis of gestational hypertension would be strengthened (*moderate*)
			• Fetal sonography (where available) should be performed to assess fetal growth, amniotic fluid volume, and umbilical artery Doppler (*moderate*). If fetal growth restriction is detected, SOGC fetal surveillance guidance should be followed[76] (*GPP*)
			Follow-up:
			Fetal sonography (where available) should be repeated at least monthly to assess fetal growth, amniotic fluid volume, and umbilical artery Doppler (*moderate*)

Preeclampsia	Gestational hypertension with new-onset proteinuria or one/more adverse conditions (defined as a maternal end-organ complication or evidence of uteroplacental dysfunction[a]) (*high*)	Diagnosis: Women should undergo comprehensive testing for preeclampsia (*high*) Maternal testing should include, in addition to gestational age and the presence of chest pain/dyspnea (*high*):[b] • oxygen saturation • platelet count • serum creatinine • AST or ALT Follow-up: Maternal testing, at least twice weekly, should include re-evaluation of (*moderate*): • gestational age • chest pain or dyspnea • oxygen saturation • platelet count • serum creatinine • AST or ALT Upon admission to delivery suite, women with preeclampsia should have a platelet count done (*GPP*)	Diagnosis: Angiogenic markers (if available) could be performed; if there is angiogenic imbalance,[c] the diagnosis of preeclampsia would be strengthened (*moderate*) Fetal sonography (where available) should be performed to assess fetal growth, amniotic fluid volume, and umbilical and uterine artery Doppler (*moderate*). If fetal growth restriction is detected, SOGC fetal surveillance guidance should be followed[76] (*GPP*) Follow-up: There is insufficient evidence to recommend re-evaluation with angiogenic markers (*very low*). Where available, fetal sonography should be performed once every 2 weeks to assess fetal growth, and at least once every 2 weeks to assess amniotic fluid volume and umbilical artery Doppler (*moderate*).

Continued

Table 2. Continued

	Definition	Maternal surveillance	Feto-placental surveillance
Superimposed on chronic hypertension	Development of 1 or more characteristics of preeclampsia (i.e., new-onset proteinuria or 1 or more adverse conditions,[a]) superimposed on chronic hypertension (*high*)	Diagnosis and follow-up should be undertaken as for women with de novo preeclampsia, above (*high*)	

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[a]For a list of the adverse conditions, see Table 4.

[b]Adverse maternal outcomes can be predicted by evaluating these components of the fullPIERS model. See text for details.

[c]Criteria for angiogenic imbalance is specific to the local assay in use.

ALT: alanine aminotransferase; AST: aspartate aminotransferase; BP: blood pressures; GPP: good practice point; SOGC: Society of Obstetricians and Gynaecolgists of Canada.

Severe hypertension is associated with an elevated risk of adverse maternal and perinatal outcomes and is a considered a medical urgency requiring antihypertensive therapy (see below).

Transient hypertension in antenatal care is associated with a 40% risk of progression to persistent hypertension,[10] warranting additional monitoring. Ideally, this would include out-of-office BP monitoring. Transient hypertension may be associated with anxiety or the pain of labour.

White-coat hypertension is common (found in approximately 30% of elevated BP before 20 weeks gestation) and is associated with an increased risk of preeclampsia,[11-13] which is intermediate between the risk among women with persistent hypertension and those with normal BP. If out-of-office BP values are normal but office values are elevated, it is reasonable not to start antihypertensive therapy.

Masked hypertension may be more common in early pregnancy (found in approximately 30% of cases compared with approximately 10% of cases outside pregnancy).[14] It should be suspected when women have manifestations associated with an HDP (i.e., maternal end-organ complications or uteroplacental dysfunction) but normal office BP. If it is detected during pregnancy, masked hypertension increases the risk of preeclampsia.[15]

Box 1. Definitions of settings for blood pressure measurement in pregnancy

Setting	Definition
Office	• Clinic • Obstetrical day unit (serial measurement) • Triage • Hospital inpatient
Out-of-office	• Home • 24-hour ambulatory blood pressure monitoring • Pharmacy

Proteinuria Measurement

Proteinuria testing at antenatal appointments for normotensive pregnant women is of uncertain value. First, dipstick proteinuria testing for preeclampsia has low diagnostic accuracy,[16] and it is rare for women to present with proteinuria before the hypertension of preeclampsia.[17] A urine protein:creatinine ratio (PCR) test at a first visit accurately excludes clinically significant proteinuria. Second, some experts question the wisdom of devoting resources to routine proteinuria screening at each antenatal visit, given that the vast majority of screening tests, at least for low-risk women, will be negative.[18]

In contrast, proteinuria testing is essential when assessing a woman with hypertension. Definitive testing for proteinuria (by urinary PCR, albumin:creatinine ratio [ACR], or 24-hour urine collection) should be performed when preeclampsia is suspected. Testing should involve more than 1 dipstick and should be performed in women with hypertension and rising BP and in women with normal BP but symptoms or signs suggestive of preeclampsia.

Classification

The HDP definitions in Table 2 distinguish among groups of women with different diagnostic and therapeutic considerations.

Chronic (Pre-Existing) Hypertension

Women with chronic hypertension who are planning a pregnancy should have their BP managed following Hypertension Canada's Guidelines for Adults.[5] Pre-pregnancy counselling may help to educate women about the risks of

chronic hypertension in pregnancy, therapies to reduce the risks of preeclampsia, prediction of adverse outcomes, and choice of antihypertensive agent.

Chronic hypertension may be associated with an increased risk of major malformations,[19,20] and these malformations do not appear to be related to antihypertensive medication in general or from any specific class. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs) can be continued in women planning pregnancy[21-23] if there is a compelling indication, such as renal protection (such as for chronic kidney disease [CKD] with proteinuria), and especially if the woman has subfertility. However, both ACE inhibitors and ARBs should be discontinued once pregnancy is determined because of their known fetotoxicity.

It may be useful to evaluate target organ damage in women with chronic hypertension if such evaluation was not conducted before pregnancy.[24] Investigations may include serum creatinine and urine protein measurement (see the earlier section on proteinuria), as well as an electrocardiogram or echocardiogram, as clinically indicated.[5,24] Liver aminotransferases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) may identify the presence of steatohepatitis in women with obesity and serve as a baseline for comparison if preeclampsia is suspected later in pregnancy. Other cardiovascular risk factors tested for outside pregnancy are either part of other routine antenatal care (hyperglycemia for gestational diabetes) or are not performed because they can be elevated in normal pregnancy (lipid profile).

Additional investigations for secondary causes of hypertension may be considered on an individualized basis, taking into consideration medical history (e.g., hypertension that is difficult to control with multiple agents, health behaviours), clinical symptoms (e.g., palpitations, snoring, heat intolerance), family history of hypertension diagnosed at a young age, or findings on physical examination (e.g., central obesity, edema) (Table 3).[25] The physiologic changes of pregnancy may affect interpretation of non-pregnant reference ranges. Consequently, a hypertension specialist should guide investigations and specific management.[24]

RECOMMENDATIONS 1, 2

Gestational Hypertension and Preeclampsia

The definitions of gestational hypertension and preeclampsia are similar to those in the 2014 guideline, with 2 exceptions. First, SOGC now recommends incorporating angiogenic markers, if available, because they reflect placental dysfunction at the core of the pathogenesis of preeclampsia and strengthen diagnosis by better identifying women and babies at risk of adverse outcomes.[26] This is an evolving field of investigation; there are many assays, and few are available in clinical practice at present. However, more specific criteria are expected to emerge in the future. Second, the SOGC no longer recommends use of the term "severe preeclampsia," as there is no consistently applied definition in use. Rather, the SOGC recommends identifying women with preeclampsia who require delivery, as outlined in Table 4.

Maternal Assessment. There are many clinical and laboratory predictors of adverse maternal outcome in preeclampsia.[27] Maternal assessment should be performed, at minimum, twice weekly, and include the components predictive of adverse maternal outcomes in hypertensive pregnancies (Table 2).[28-30]

The Preeclampsia Integrated Estimate of Risk Score (PIERS) is a model of clinical and laboratory variables that predict which women are most likely to experience adverse maternal outcomes once preeclampsia has been diagnosed.

The externally validated fullPIERS model includes the following variables: gestational age, chest pain/dyspnea, pulse oximetry, platelet count, serum creatinine, and AST or ALT.[29,31,32] The fullPIERS model incorporates gestational age but is not restricted to a specific gestational age range, which differs from the Prediction of Complications in Early-Onset Preeclampsia (PREP) model developed for use in preeclampsia before 34 weeks gestation.[33] The model does not include proteinuria; once confirmed as meeting criteria, proteinuria testing does not need to be repeated. (See BP and proteinuria, Table 1, for further details.)

In self-monitored or some outpatient settings where laboratory testing is not available, the miniPIERS model includes the following variables that increase risk: higher systolic BP, proteinuria (determined by dipstick testing), nulliparity, earlier gestational age, and symptoms (headache/visual symptoms, chest pain/dyspnea, and abdominal pain with vaginal bleeding); the model's performance is improved by adding pulse oximetry.[28,34]

The assessment of clonus is generally not recommended. While it reflects central nervous system irritability, and it has been used in trials to determine eligibility for magnesium sulphate therapy,[35] its reproducibility in maternity care and its independent predictive value for adverse

Table 3. Secondary hypertension in pregnancy

Secondary hypertension	Clinical features	Investigations	Considerations for pregnancy
Obstructive sleep apnea (OSA)	• Higher BMI • Snoring, daytime somnolence • Witnessed apneas during sleep	• Home sleep study • Overnight polysomnography	• OSA may worsen due to edema in upper airways • Untreated OSA associated with increased risk of preeclampsia
Renovascular disease (i.e., renal artery stenosis, fibromuscular dysplasia)	• Age of onset <30 y • Sudden worsening of hypertension • Difficult-to-control hypertension (≥3 antihypertensives) • Abdominal bruit • Sudden pulmonary edema • Family history	• Creatinine • Renal sonography (asymmetry)	Other investigations considered post-pregnancy (CTA, MRA, captopril-enhanced radioisotope renal scan) due to fetal risks of exposures[a]
Renal parenchymal disease	• Autoimmune disorders (e.g., vasculitis, lupus erythematosus) • Pre-pregnancy diabetes • Family history	• Creatinine • Urinalysis (proteinuria, hematuria, active sediment) • Autoimmune antibodies • Renal sonography	• Presence of proteinuria may be difficult to distinguish from preeclampsia • Anti-Ro/La (SSA/SSB antibodies) may be associated with fetal heart block and neonatal lupus • Control of BP may reduce progression of kidney disease during pregnancy
Primary aldosteronism	Muscle weakness/cramps from hypokalemia	• Electrolytes (hypokalemia) • Aldosterone-renin ratio • Sonography of adrenal glands	• Pregnancy and preeclampsia substantially increase aldosterone levels • Testing as per HC 2020 Guidelines[a]
Thyroid			
Hyperthyroid	• Palpitations, heat intolerance, weight loss, tremor, etc. • Eye symptoms (Grave's disease) • Goiter	• TSH, free T4, free T3 • TSH-receptor antibodies	• β-hCG stimulates thyroid and lowers TSH • Use of trimester-specific and local reference ranges suggested
Hypothyroid	• Weight gain, cold intolerance, fatigue, etc. • Previous radiation to thyroid area	TSH, free T4, free T3	• Avoidance of radioactive iodine in pregnancy due to effects on fetal thyroid
Pheochromocytoma/ paraganglioma	• Headaches, palpitations, diaphoresis, pallor • Labile BP	• Plasma metanephrines • Urinary metanephrines and catecholamines	• Imaging of adrenals considered on an individualized basis • Pregnancy increases metanephrines • Testing as per HC 2020 Guidelines[a] • Interdisciplinary management required before delivery to prevent hypertensive crisis
Cushing's disease	Central obesity, easy bruising, fat redistribution (dorsal and supraclavicular, round face), proximal muscle weakness	• 24-hour urinary free cortisol; salivary cortisol • Dexamethasone suppression tests	• Screen for associated dysglycemia • Abdominal or pituitary imaging considered on individualized basis
Hypercalcemia	Polyuria, polydipsia, nausea, weakness, confusion	Calcium, albumin	Lowered albumin levels in pregnancy

Continued

Table 3. Continued

Secondary hypertension	Clinical features	Investigations	Considerations for pregnancy
Coarctation of aorta	• Asymmetric BP in arms • Increased BP in upper > lower extremities • History of congenital heart disease	Echocardiogram	• Other maternal imaging (MRI, CT) considered on individualized basis • Increased fetal risks of congenital heart disease; consider fetal echocardiogram
Drugs	• Antidepressants (SNRIs, tricyclics) • Steroids • Sympathomimetics (cocaine, amphetamines) • Herbal substances	Drug screen as indicated	Consider discontinuation on an individualized basis

Adapted from Unger et al.[25] and Rabi et al.[5]

[a]Refer to Hypertension Canada 2020 guidelines for details of investigations of hyperaldosteronism and pheochromocytoma.[5]

β-hCG: beta human chorionic gonadotropin; BMI: body mass index; BP: blood pressure; CT: computed tomography; CTA: computed tomography angiography; HC: Hypertension Canada; MRA: magnetic resonance angiography; MRI: magnetic resonance imaging; SNRI: selective norepinephrine and serotonin reuptake inhibitors; SSA/SSB: anti-Sjogren's syndrome A/B; TSH: thyroid-stimulating hormone.

outcomes are uncertain. Serum uric acid testing is not recommended, but, if it is performed and uric acid is found to be increased after correction for gestational age, increased fetal surveillance is warranted[36,37] (see the following section on fetal assessment).

It is unknown whether angiogenic markers may add to prediction of adverse outcomes among women with preeclampsia, over and above maternal (fullPIERS) variables listed above; this issue is complicated further by varied definitions of "suspected preeclampsia," including proteinuria or fetal components in isolation, and varied prognostic performance.[38,39] Further exploration is warranted.[40]

Fetal Assessment. While multiple methods of fetal surveillance are available, no strategy of various methods and timing has been recognized to be superior to others, in general or in hypertensive pregnancy specifically. At present, there is no validated model of tests of fetal well-being to predict adverse perinatal outcomes in hypertensive pregnancy.

Elevated serum uric acid corrected for gestational age is associated with increased perinatal risk and placental dysfunction, but its usefulness in practice, along with other clinical, laboratory, and sonographic variables, is unclear. Thus, uric acid testing is not routinely recommended. Further, while hyperuricemia alone is not an indication for delivery, it is associated with placental dysfunction and increased perinatal risk, so increased fetal surveillance is reasonable.

Sonographic assessment of fetal growth and amniotic fluid volume is recommended, as a fetus with growth restriction and/or reduced amniotic fluid volume is at particular risk of stillbirth and neonatal mortality and morbidity. Doppler sonography of the umbilical artery may reduce perinatal death and obstetric intervention in high-risk pregnancies, but the evidence is not definitive.[41] Near or at term, a normal umbilical artery Doppler sonographic examination does not exclude fetal compromise. At <34 weeks gestation, if there is fetal growth restriction, performing Doppler velocimetry of the ductus venosus may be helpful; absent or reversed "a-wave" is associated with a substantially increased risk of stillbirth.[42] Neurodevelopmental outcome among survivors is improved when timing of birth is based on abnormal ductus venosus Doppler or spontaneous fetal heart rate (FHR) decelerations (or short-term FHR variability by computerized cardiotocograph).[43] Relying solely on the biophysical profile to monitor pregnancies complicated by hypertension and fetal growth restriction is not recommended, as changes in the biophysical profile that reflect fetal compromise are a late finding.[44]

When the care provider does not have ready access to methods of fetal surveillance beyond FHR monitoring, maternal characteristics can be used to estimate perinatal risk at ≥32 weeks gestation; before this time, perinatal risk is almost entirely driven by gestational age.[45]

PREDICTION

The sensitivity of clinical risk factors for preeclampsia (that develops preterm or at term) is low (<40%),[46] but using these risk factors as the basis of treatment with low-dose acetylsalicylic acid to prevent preterm preeclampsia is likely to be effective (Box 2).

Table 4. Adverse conditions that define preeclampsia together with hypertension

	Follow closely regarding need for delivery (Fig 1)	Deliver regardless of gestational age
Maternal end-organ dysfunction		
CNS	Severe headache/visual symptoms	• Eclampsia • PRES • Cortical blindness or retinal detachment • Glasgow coma scale <13 • Stroke, TIA, or RIND
Cardiorespiratory	• Chest pain/dyspnea[a] • Oxygen saturation <97[a]	• Uncontrolled severe hypertension (over a period of 12 hours despite use of 3 antihypertensive agents) • Oxygen saturation <90%, need for ≥50% oxygen for >1 hour, intubation (other than for cesarean section), pulmonary edema • Positive inotropic support • Myocardial ischemia or infarction
Hematological	Low platelet count[a]	• Platelet count $<50 \times 10^9$/L • Transfusion of any blood product
Renal	Elevated serum creatinine[a]	• Acute kidney injury (creatinine >150 μM with no prior renal disease) • New indication for dialysis
Hepatic	• RUQ or epigastric pain • Elevated serum AST[a], ALT	• Hepatic dysfunction (INR >2 in absence of DIC or warfarin) • Hepatic haematoma or rupture
Uteroplacental dysfunction	• Atypical or abnormal NST/CTG • FGR • Oligohydramnios • Absent or reversed end-diastolic flow by umbilical artery Doppler velocimetry • Angiogenic imbalance[b]	• Abruption with evidence of maternal or fetal compromise • Absent or reversed ductus venosus a-wave by Doppler velocimetry • Intrauterine fetal death

[a]Along with earlier gestational age, these factors are independently predictive of adverse maternal outcome in preeclampsia.[29,31]

[b]Angiogenic imbalance includes, for example, a soluble fms-like tyrosine kinase-1:placental growth factor ratio of >85 by the Roche assay.

ALT: alanine aminotransferase; AST: aspartate aminotransferase; CTG: cardiotocography; DIC: disseminated intravascular coagulation; FGR: fetal growth rate; INR: international normalized ratio; NST: non-stress test; PRES: posterior reversible leukoencephalopathy syndrome; RIND: reversible ischemic neurological deficit <48 hours; RUQ: right upper quadrant; TIA: transient ischemic attack.

The risk factors have been based on those that can be assessed in early pregnancy and are amenable to risk reduction by low-dose acetylsalicylic acid,[47] prescribed for women with 1 high-risk or more than 1 moderate-risk factor. However, CKD has been listed as a high-risk (rather than moderate-risk) factor because of the wide spectrum of CKD seen in practice and its demonstrated relationship to adverse outcomes,[48] compared with the narrow range of CKD considered in the published cohort studies.[47] There are also some differences in designation of factors as high- or moderate-risk compared with other publications; of note, the 2019 SOGC Pregnancy and Maternal Obesity Guideline regarded obesity as a moderate-risk factor.[49]

Given the prevalence of obesity, addressing the risk of preeclampsia associated with it could have a meaningful impact on preeclampsia incidence.[47] While obesity is often associated with other preeclampsia risk factors, obesity is also an independent risk factor, according to the Fetal Medicine Foundation (FMF) model, discussed further on in this guideline.[46] The FMF model includes the factors listed in Box 2, with a few exceptions. Excluded are CKD and, for parous women, prior abruption and fetal growth restriction. Additional historical factors are racial origin, smoking (protective), family history of preeclampsia, and, for parous women, interpregnancy interval and prior gestational age at delivery.[50]

Combining clinical (maternal risk markers), biochemical (e.g., placental growth factor [PlGF]), and sonographic risk markers (uterine artery pulsatility index) at 11−14 weeks gestation is a better way to identify women at increased risk of preeclampsia. Combining markers has sensitivities of 75% for preterm preeclampsia and 47% for term preeclampsia, compared with sensitivities of 34% and 39%, respectively, for use of clinical risk markers alone,[46,51] and of about 70% for use with either PlGF or uterine artery pulsatility index.[46,51] No additional value is offered by pregnancy-associated plasma protein A in the absence of

Box 2. Clinical risk factors for preeclampsia that can be identified in early pregnancy[a]

	High risk factors (any 1)	Moderate-risk factors (2 or more)
Pregnancy history	Prior preeclampsia	• Prior placental abruption • Prior stillbirth • Prior FGR
Demographics	Pre-pregnancy BMI >30 kg/m^2	Maternal age >40 y
Pre-existing medical conditions	• Chronic hypertension • Pre-gestational diabetes mellitus • Chronic kidney disease[b] • Systemic lupus erythematosus/antiphospholipid antibody syndrome[b]	
Current pregnancy	Assisted reproductive therapy	• Nulliparity • Multifetal pregnancy

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[a]Women are considered to be at increased risk of preeclampsia if they have at least 1 high-risk factor, or at least 2 moderate-risk factors.

[b]Listed as high-risk (rather than moderate risk as in Bartsch *et al*[47]).

BMI: body mass index; FGR: fetal growth rate.

PlGF. An online calculator is available.[50] While a combined approach may not be feasible based on local resources, its use as the basis for acetylsalicylic acid therapy (150 mg each night) is effective in decreasing the risk of preterm preeclampsia[52] (see section on prevention for details).

While mid- or late-pregnancy re-screening for preeclampsia risk may provide further benefits through increased maternal-fetal surveillance or timed delivery, there is insufficient evidence on such a tiered approach to guide recommendations. An individualized approach should be undertaken.

RECOMMENDATIONS 3, 4

PREVENTION

Table 5 provides a unified approach to prevention, accounting for risk of preeclampsia.

Acetylsalicylic Acid

There are no trials comparing a daily doses of acetylsalicylic acid (ASA) of 81 mg (or a similar, lower dose) and 162 mg (or a similar, higher dose). A daily dose of 162 mg (or at least 100 mg) would maximize effectiveness, whereas a daily dose of 81 mg would maximize maternal safety. Based on the evidence, the guideline authors were unable to reach consensus on a single recommended dose. Therefore, the daily dose should be individualized, based on discussion with the woman, the care provider's predominant concerns, and individual characteristics, such as obesity, twin pregnancy, or bleeding risk. In Canada, low-dose ASA is available only in 81 mg tablets. While it is impossible to cut enteric-coated pills, some practitioners give more tablets on some days of the week to achieve an averaged dose of at least 100 mg/d or close to 150 mg/d.

In the recent ASPRE trial of women with singleton pregnancies who were at high risk of preeclampsia based on multivariable first-trimester screening, 150 mg of ASA (vs. placebo) taken at bedtime was associated with good adherence (approximately 80%) and a reduction in preterm (but not term) preeclampsia by 62% (to 1.6%, compared with 4.3% in the placebo group).[52] A daily dose of 81 mg may be less effective, based on platelet insensitivity, in up to approximately 40% of women, particularly as pregnancy progresses and in women with a higher body mass index.[53,54]

Although ASA has not been associated with miscarriage, recent literature continues to raise concerns about small potential risks, even at a 75 mg daily dose, but probably higher with increasing dosage.[55] Adverse effects may include vaginal spotting;[56,57] antepartum,[58,59] intrapartum,[60] and postpartum hemorrhage;[56,59,60] postpartum hematoma;[60] and a small (0.06%) absolute increase in neonatal intracranial hemorrhage,[60] particularly after vaginal birth.[60] (These are in addition to the rare risks of extracranial bleeding in otherwise healthy individuals.) Many risks may be mitigated by discontinuing ASA by 36 weeks because of its lack of effectiveness for prevention of term preeclampsia.[61] Such risks are tiny compared with the benefits of ASA

Table 5. Recommendations for preeclampsia prevention according to clinical risk

Prevention	Women at increased risk[a] of preeclampsia	All other women
Low-dose ASA	Low-dose ASA (81 or 162 mg/d) is recommended (strong, high), to be taken at bedtime (strong, moderate), preferably before 16 weeks (conditonal, moderate), and discontinued by 36 weeks (*conditional, low*)	Low-dose ASA is not recommended (*strong, moderate*)
Calcium	For women with low dietary intake of calcium (< 900 mg/d), oral calcium supplementation of at least 500 mg/d is suggested (*conditional, low*)	Same as for women at increased risk[a] of preeclampsia
Vitamin D	Vitamin D supplementation over and above Health Canada's recommendation for adults is not suggested for preeclampsia prevention (*conditional, moderate*)	Same as for women at increased risk[a] of preeclampsia
Exercise	Exercise is recommended for preeclampsia prevention (*strong, moderate*)	Same as for women at increased risk[a] of preeclampsia
Dietary advice	For women who are overweight or obese, dietary advice (reduced calories and food with a low glycemic index) and exercise are recommended (*conditional, moderate*)	—

[a]Increased risk has been most commonly identified by a personal or family history of an HDP or a chronic medical disease; an abnormal uterine artery Doppler before 24 weeks gestation; or, recently, the FMF algorithm. Some of these risk factors are listed in Box 2.

ASA: acetylsalicylic acid.

for women identified as being at high risk of preeclampsia; however, these risks caution against universal ASA administration, despite the apparent cost-effectiveness of this approach for all women[62,63] or all nulliparous women,[56] among whom there is a lack of demonstrated effectiveness.

Calcium

The recommended daily intake of calcium is 1000 mg/d for adult women, among whom inadequate calcium intake is common (in 48%–87%). The recommended daily intake of calcium for pregnant women is 1300 mg/d (but not more than 3000 mg/d), and, for lactating women, 1000 mg/d (but not more than 2500 mg/d).[64]

At a population level, low dietary intake of calcium is associated with a higher incidence of pregnancy hypertension. In populations with low dietary intake (<900 mg/d), and particularly among women at high-risk, high-dose calcium supplementation from 20 weeks gestation (at a dose of at least 1000 mg/d) may reduce the risk of both preeclampsia and preterm birth.[65] Among women with prior preeclampsia, calcium supplementation of 500 mg/d before pregnancy, and up to 20 weeks' gestation of the subsequent pregnancy (followed by 1.5 g/d thereafter) reduced the incidence of preeclampsia, but only when compliance with tablets to 20 weeks was at least 80% (relative risk [RR] 0.66; 95% confidence interval [CI] 0.44–0.98), and reduced the incidence of pregnancy loss or preeclampsia (RR 0.82; 95% CI 0.66–1.00).[66]

Vitamin D

Women should comply with Health Canada's recommendation that adults take at least 600 IU of vitamin D per day (but not exceed 4000 IU daily) to prevent vitamin D deficiency.[64] However, to date, there are uncertainties about the effectiveness of additional vitamin D and its dosage for preeclampsia prevention and concerns that such supplementation may increase preterm birth.[67,68]

Lifestyle Change

In randomized trials, exercise reduced the risks of both gestational hypertension (odds ratio [OR] 0.61; 95% CI 0.43–0.85) and preeclampsia (OR 0.59; 95% CI 0.37–0.90) (as well as gestational diabetes; OR 0.62; 95% CI 0.52–0.75).[69,70] To achieve a reduction of 25% in the odds of developing gestational hypertension or preeclampsia, pregnant women must accumulate at least 140 minutes per week of moderate-intensity exercise—activity that noticeably increases heart rate during which a person can talk but not sing (e.g., brisk walking, water aerobics, stationary cycling with moderate effort, resistance training, carrying moderate loads, and household chores such as gardening or washing windows).

A lifestyle intervention of diet and exercise for women who are overweight or obese may reduce preeclampsia and gestational hypertension (as well as gestational diabetes), but data from randomized controlled trials are lacking for hypertension and have shown that such an intervention is ineffective for gestational diabetes.[71-73]

Other

Women are not recommended to take high-dose folic acid beyond the first trimester[74] or vitamin C and E for prevention of preeclampsia. The effectiveness of heparin remains uncertain.[75] There is insufficient evidence to make recommendations about using dietary salt restriction, omega-3 fatty acids, or thiazide or thiazide-like diuretics for preeclampsia prevention.

RECOMMENDATIONS 5, 6, 7, 8, 9, 10

MANAGEMENT

Place of Care

Preeclampsia can progress quickly and is associated with an increased risk of adverse maternal and/or fetal outcomes. As such, inpatient care should be provided for women with an adverse maternal condition(s) (Table 4). Indications for hospital admission based on fetal adverse conditions should comply with each unit's fetal surveillance policies.[76]

A component of care outside hospital can be considered for women with non-severe hypertension (regardless of pregnancy hypertension type) or preeclampsia with proteinuria but without maternal adverse conditions. However, criteria for outpatient care should be clear within a given centre. Considerations include reasonable home-to-facility distance, ready access to maternal and fetal surveillance, patient compliance and reliability, an experienced and well-organized team, well-controlled hypertension, and no evidence of significant disease progression (maternal or fetal). Where women with preeclampsia are given care, resources should be available to provide urgent delivery and acute care of sick women and newborns.[77] Consultation with the regional referral centre should be considered.

Outpatient management could take the form of home care, for example, although regular (ideally daily) contact (in person or virtually) is necessary to ensure that the mother and fetus are doing well and that the preeclampsia has not progressed. A home care program must have clear criteria for eligibility, and those overseeing care must be knowledgeable about hypertensive disorders of pregnancy.

RECOMMENDATION 11

Transport

In a country as vast as Canada, health care is regionalized. This may necessitate transfer of women with HDPs, particularly when women have preeclampsia or its complications, or may require preterm delivery. It is essential that each maternity unit have an agreement and a predetermined process with the regional referral centre for such care and transfer.[78]

Good communication is an essential component of patient transfer. There should be direct, documented communication between the referring health care provider and the accepting physician. A copy of the maternal records must accompany the patient. The contact number for the receiving site must be clear so that any change in maternal condition during transport can be communicated before arrival. Finally, the transport team and receiving physician should provide a debriefing to the woman and family.

Box 3 lists the issues specific to HDP to consider for transfer. Any maternity transfer should have a delivery bundle as essential equipment.

Maternal Activity

Bed rest is variably defined, and there are limited trial data to inform practice. For preeclampsia, strict (vs. some) bed rest in hospital does not alter outcomes.[79] In 1 trial involving 218 women with gestational hypertension, some bed rest in hospital (vs. routine activity at home) decreased severe hypertension (RR 0.58; 95% CI 0.38—0.89) and preterm birth (RR 0.53; 95% CI 0.29—0.99), but it was unclear whether the hospitalization, bed rest, or both may have been responsible for benefits.[79] In the absence of clear benefits, and in the face of potential harms (physical, psychosocial, or financial), bed rest cannot be recommended.

There is insufficient evidence to make recommendations about dietary and lifestyle interventions (e.g., guided imagery) for management of preeclampsia.[80] Uncontrolled hypertension of any type—and preeclampsia specifically—are absolute contraindications to exercise.[69]

RECOMMENDATION 12

Antihypertensives

The Control of Hypertension In Pregnancy Study (CHIPS) showed that a target office diastolic BP of 85 mm Hg (vs. 100 mm Hg) halves the risk of severe hypertension,

Box 3. Transport checklist for women with preeclampsia

	Factor to consider	Specifics
☐	Maternal condition has been stabilized	• BP <160 mm Hg systolic, <110 mm Hg diastolic • Antihypertensive medications initiated if needed • Patient is responsive and following commands or intubated and ventilated • IV access established • Foley catheter considered
☐	Fetal condition has been assessed and documented	• Fetal heart rate has been documented as present or absent • If fetal heart rate is present, there is no fetal indication for delivery before transport
☐	Eclampsia prophylaxis if indicated	• Consider IM $MgSO_4$ for safety during transport (5 g IM into each buttock, with consideration of adding to the injection 2 mL xylocaine 1% without epinephrine, or administering xylocaine 2 minutes before injections) • Calcium gluconate (10 mL of 10% solution IV over 3 min)
☐	Accompanying health care provider has necessary skills and qualifications	• Monitor BP and reflexes hourly • Administer antihypertensive medications to keep BP <160/110 mm Hg[135] • Manage seizures (prevent aspiration, protect tongue, ventilate, administer $MgSO_4$) • Ventilate if apnea occurs, or SpO_2 drops to <90% and is unresponsive to supplemental oxygen • Document FHR immediately before departure and upon arrival
☐	Additional doses of antihypertensive medication and IV $MgSO_4$ available (for management of eclampsia)	• Oral nifedipine 5 mg capsules or • Oral labetalol 200 mg tablets • $MgSO_4$ 4 g IV over 5 min
☐	Confirm the following with receiving centre as indicated	• Need for tocolysis • Antenatal corticosteroids initiated, if conditions dictate, in pregnancy $\leq 34^6$ weeks

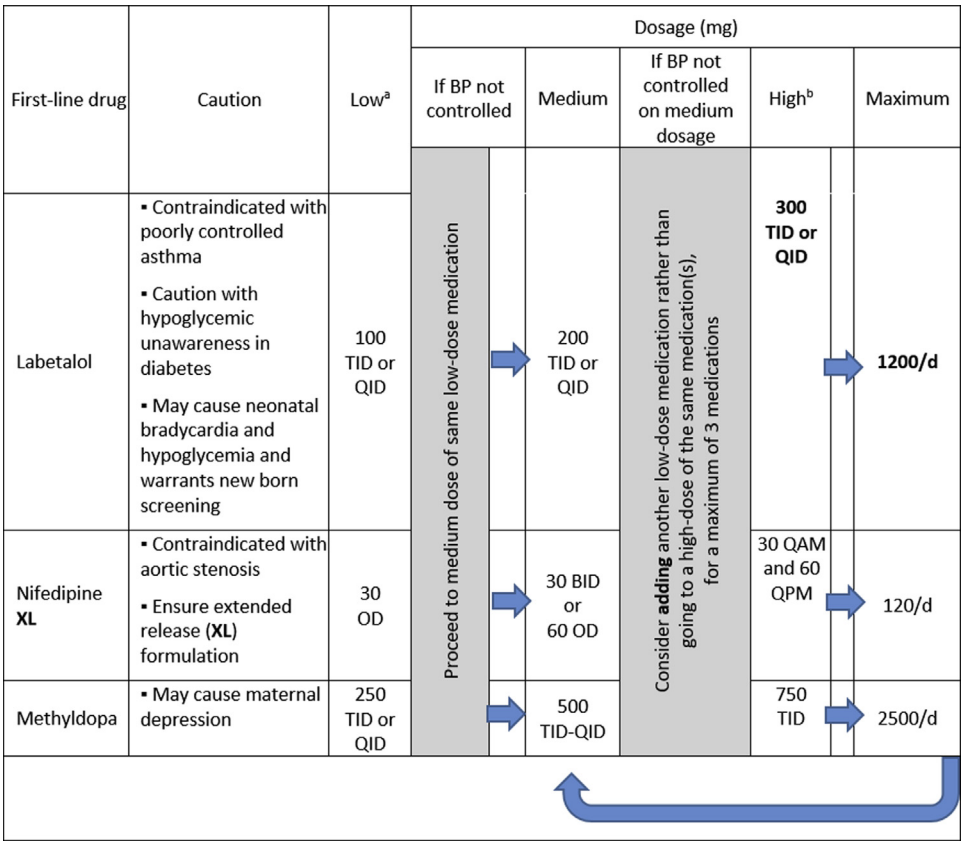
BP: blood pressure; FHR: fetal heart rate; IM: intramuscular; IV: intravenous; SpO_2: oxygen saturation; $MgSO_4$: magnesium sulphate.

without increasing the risk of perinatal mortality or morbidity.[81] While the trial enrolled only women with chronic or gestational hypertension, women who progressed to preeclampsia remained in the allocated group, and the results are considered to apply to them.[82-84] Based on CHIPS, Hypertension Canada also recommends that all hypertension in pregnancy be treated with antihypertensive therapy; a target systolic BP was not specified in CHIPS, but the systolic BP achieved was 133 mm Hg.[81] Increased use of antihypertensive medication in hospitalized patients with preeclampsia has been associated with a reduced incidence of stroke.[85]

As previously mentioned, BP measured out-of-office is generally lower than office BP values among hypertensive women. However, there is wide variation and a lack of consensus about whether an out-of-office BP target should be 130/80 mm Hg (corresponding to an office value of 135/85 mm Hg) or 135/85 mm Hg (corresponding to an office BP value of 140/90 mm Hg).[9] It should certainly be no higher than the latter.

Initial antihypertensive therapy in pregnancy should be monotherapy, with the drug chosen from among the following first-line drugs (according to small randomized trials): oral labetalol, oral methyldopa, long-acting oral nifedipine, or other oral beta-blockers (acebutolol, metoprolol, pindolol, or propranolol)[86] (Figure 1). ACE inhibitors or ARBs that the patient was taking when the pregnancy was confirmed should be discontinued and replaced with a different class of antihypertensive agent. For chronic hypertension, specifically, a recent network meta-analysis found that methyldopa and nifedipine each significantly decreased both severe hypertension and abruption, while atenolol increased the risk of small for gestation age infants.[87] The choice of antihypertensive agent should be based on characteristics of the patient (e.g., risk of hypoglycemia, side effects, or hemodynamic profile, if assessed),

Figure 1. Maintenance therapy and suggested dose titration of antihypertensive therapy for non-urgent control of hypertension in pregnancy.



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[a] Starting doses are higher than generally recommended for adults, given more rapid clearance in pregnancy.
[b] When a medication is at high (or maximum) dosage, consider using a different medication to treat any severe hypertension that may develop.
Source: adapted from ALARM 27th Edition ALARM Manual, Table 8 of the SOGC 2014 guideline and Magee et al.[136]
OD: once daily; TID: 3 times daily; QAM: every morning; QID: 4 times daily; QPM: every evening.

contraindications to a particular drug, and physician and patient preference.[88]

Caution should be exercised when using labetalol or other beta-blockers in women with asthma, particularly if asthma is not well-controlled, given the slight (about 0.5%) increased risk of status asthmaticus.[89] The Canadian Paediatric Society recommends screening for neonatal hypoglycemia following maternal labetalol use,[90] although it is not known whether acute and chronic use, or oral and parenteral administration carry the same risk.

While no antihypertensive medication is proven to be teratogenic, there are lingering concerns that hypertension itself may be.[91] No firm conclusions can be drawn with regard to long-term child outcomes, given the paucity of relevant high-quality studies.[92]

Hypertension Canada recommends that additional antihypertensive drugs be used if target BP levels are not achieved with standard-dose monotherapy; add-on drugs should be from a different drug class chosen from first-line or second-line options (Figure 1).[82]

The following are considered second-line options because of concerns about potential side effects: clonidine, hydralazine, and thiazide diuretics. There is insufficient data in pregnancy to recommend amlodipine.

When BP is severely elevated, antihypertensive therapy should be administered within 60 minutes to decrease the risk of severe maternal morbidity[93] (Figure 2). The antihypertensive choices listed in Figure 2 all lower BP in the majority (at least 75%) of women;[94-96] oral methyldopa may more often require adding another antihypertensive.[97]

Figure 2. Suggested dose titration of antihypertensive therapy for urgent control of hypertension in pregnancy[a].

Drug	Caution	T 0 min	T 30 min	T 60 min	T 90 min	T 120 min	T 150 min	T 180 min
Labetalol (oral)	• Contraindicated in patients with uncontrolled asthma or heart failure • Caution with hypoglycemic unawareness in diabetes • May cause neonatal bradycardia and neonatal hypoglycemia and warrants newborn screening	200 mg	—	200 mg	—	200mg	—	Use alternative from a different drug class[d]
Labetalol (IV intermittent)		10–20 mg	20–40 mg[b]	40–80 mg	40–80 mg	40–80 mg	40–80 mg[c]	
Labetalol (IV infusion)		0.5–2 mg/min	→	→	→	→	→[d]	
Nifedipine (oral capsule swallowed whole, *not* bitten or punctured)	• May cause maternal headache and tachycardia	5-10 mg	10 mg	—	10 mg	—	10 mg	
Methyldopa (oral)	• Onset of action may be delayed	1000 mg	—	—	—	—		
Hydralazine (IV)	• May increase risk of maternal hypotension, and maternal and fetal tachycardia	5 mg	5–10 mg	5–10 mg[e]	5–10 mg[e]			

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[a] When severe hypertension has resolved, switch to routine oral medication.
[b] Double the initial dose of labetalol IV.
[c] Do not exceed the maximum dose of IV labetalol, which is 300 mg total in a treatment course.
[d] If nifedipine or hydralazine were the initial drug used, choose oral labetalol or oral methyldopa as the alternative.
[e] Do not exceed the maximum dose of IV hydralazine of 20 mg.
IV: intravenous.

If women are already taking daily medication, it is best to add a drug from a different drug class to treat severe hypertension, as for non-severe hypertension.[82] While all women with severe hypertension have an obstetric urgency, oral therapy may facilitate earlier therapy en route to, or within, a facility. Local protocols should be in place for maternal monitoring, intravenous access, and fetal monitoring. If BP is not adequately controlled, when to repeat a dose of antihypertensive medication varies by drug and route of administration. In the absence of an emergency (such as an aortic dissection) in the intensive care setting, 30 minutes after parenteral labetalol, hydralazine, or oral nifedipine, and 60 minutes after other oral medication, is a reasonable interval and unlikely to result in maternal hypotension. Nifedipine and magnesium sulphate can be used at the same time.[98] However, magnesium sulphate alone is not recommended as an antihypertensive agent.

RECOMMENDATIONS 13, 14, 15

Magnesium Sulphate

Although magnesium sulphate can benefit all women with preeclampsia, the drug has its greatest impact among women with severe hypertension or adverse maternal conditions who are at highest risk of, and who expereince, eclampsia (Table 3).[99,100] Figure 3 summarizes suggested magnesium sulphate dosage and monitoring. While alternative regimens (lower in dosage or more restricted in duration) have been evaluated, data are insufficient to inform recommendations for practice.[101]

All centres should have a standard protocol for clinical monitoring of women receiving magnesium sulphate, such as hourly assessment of urine output, respiratory rate, and reflexes. Monitoring of serum magnesium levels is not necessary unless there is evidence of toxicity or women are at particular risk of toxicity, such as women with renal insufficiency.[102] The antidote for toxicity is calcium gluconate 10%, 1 ampule (10 mL) IV over 3 minutes.

When not indicated for seizure prophylaxis, administration of magnesium sulphate for fetal neuroprotection should be considered according to current SOGC guidance, when delivery is imminent at $<33^{6}$ weeks gestation.[103]

RECOMMENDATION 16

Figure 3. Magnesium sulphate dosage and monitoring.

Dosage[35, 136]	IV administration	Combined IV and IM administration[a]
Loading dose	4 g $MgSO_4$ IV in 100 mL normal saline solution, infused over 20 min using an infusion device	4 g $MgSO_4$ IV in 100 mL normal saline solution, infused over 20 min using an infusion device *and* 5 g IM into *each* buttock (for a total of 10 g), every 4 h
Maintenance	1 g/h IV in normal saline solution, using an infusion device	5 g IM into *one* buttock every 4 h
Duration	Until 24 h after last eclamptic seizure or birth, whichever is later	
Monitoring	**Observations**	**Signs of toxicity[b]**
Maternal		
Upon completion of loading dose	Reflexes	Decreased or absent
Every 30 min	BP	Lower
	Heart rate	Lower or cardiac arrhythmias
	Respiratory rate	<12/min for 15 min
	Pulse oximetry	O_2 saturation <94% for 15 min
Every hour	Urine output[d]	<30 mL/h for 4 h[e]
	Reflexes	Decreased or absent
Symptoms[f]	Central nervous system (e.g., excessive drowsiness, slurred speech)	
	Neuromuscular (e.g., muscle weakness)	
Fetal		
≥26 wk	Continuous cardiotocography	
<26 wk	Intermittent FHR auscultation every 30 min	

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[a] Administration can be switched to IV dosing by starting 1 g/h (without a loading dose) when the next dose of IM magnesium sulphate is due.
[b] Monitoring of serum magnesium levels is not necessary unless there is decreased renal function or signs of toxicity.
[c] If toxicity is suspected, cease the $MgSO_4$ infusion and take blood for serum Mg level. If toxicity is clear, administer calcium gluconate 10% (10 mL in 100 mL normal saline solution IV over 3 min).
[d] Foley catheterization is recommended.
[e] Decreased urine output is included because it increases the risk of toxicity.
[f] Symptoms of toxicity should be distinguished from well-known side effects, which include flushing of the skin, a metallic taste in the mouth, sweating, nausea and vomiting, heaviness in the chest, palpitations, and lowering of the BP initially.
BP: blood pressure; FHR: fetal heart rate; $MgSO_4$: magnesium sulphate; O_2: oxygen.

Other Aspects of Care for Women with Preeclampsia

The Team

Women with preeclampsia require multidisciplinary care. Apart from obstetrics, anesthesiology and newborn care teams should be informed when a woman with preeclampsia is admitted to the delivery suite.

Fluid Management

For women with preeclampsia, total fluid intake in labour should be restricted to about 80 mL/h based on a reduction in pulmonary edema without an increase in acute kidney injury.[104] Small randomized trials have collectively failed to show an ideal fluid strategy.[105]

Corticosteroids for HELLP Syndrome

Corticosteroids may transiently improve platelet count and other laboratory results in HELLP syndrome, but they have not demonstrated any reduction in adverse outcomes.[106,107] Hence, steroids cannot be recommended.

Antenatal corticosteroids for acceleration of fetal pulmonary maturity should be administered to women with preeclampsia at risk of preterm birth when gestational age-related criteria are met and delivery is anticipated within 7 days.[108]

Platelet Transfusion

Upon admission to delivery suite, women with preeclampsia should have a platelet count done. Counts in HELLP syndrome may fall rapidly and require frequent reassessment. Clinicians should be aware of the potential for delays when ordering platelets or other blood products. Anti-D(Rho) sensitization can be prevented by anti-D prophylaxis in Rh D-negative women.

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Table 6. Recommendations for timing of delivery

	Viability to 33^6 weeks	34^0–36^6 weeks	$\geq 37^0$ weeks
Chronic hypertension	Expectant care unless there is an indication for birth (*strong, very low*)	Same as viability to 33^6 weeks (*strong, very low*)	Initiation of delivery can be offered at 38^0 to 39^6 weeks, but should be advised from 40^0 weeks (*conditional, low*)
Gestational hypertension	Expectant care unless there is an indication for birth (*strong, low*)	Same as viability to 33^6 weeks (*strong, very low*)	For women whose gestational hypertension arose at $<37^0$ weeks, initiation of delivery can be offered at 38^0 to 39^6 weeks, but should be advised from 40^0 weeks (*conitional, low*) For women who are already at $\geq 37^0$ weeks, and then present with gestational hypertension, initiation of delivery should be discussed (strong, moderate)
Preeclampsia	Expectant management may be considered, but only in perinatal centres capable of caring for very preterm infants (*conditional, moderate*)	At 34^0–35^6 weeks, initiation of delivery should be discussed, as it decreases maternal risk but increases neonatal risk, particularly if antenatal corticosteroids are not prescribed (*strong, moderate*) At 36^0–36^6 weeks, initiation of delivery should be considered (*strong, moderate*)	Initiation of delivery is recommended (*strong, high*)

Timing of Delivery

Recommendations for timing of delivery, regardless of gestational age or whether a course of antenatal corticosteroids has been completed, are presented in Table 4. When delivery is indicated, if timing allows, it should occur in a perinatal centre capable of caring for sick mothers and neonates.

Previability, preeclampsia is associated with high perinatal mortality (>80%) and maternal complications (in 27%–71% of cases), including death.[109,110] Thus, as part of expectant care, termination of pregnancy should be discussed. (See also relevant SOGC guidance.[111])

Timed birth, according to gestational age, is presented in Table 6. At $<34^0$ weeks, when there are no indications for birth (Table 4), expectant care (compared with intervention) is associated with similar short-term maternal outcomes but less neonatal morbidity, despite more babies being born small for gestational age (data from 6 trials involving 748 women).[112] Expectant care should be undertaken only in perinatal centres capable of caring for sick mothers and very preterm infants.

At 34^0 to 35^6 weeks gestation, the maternal benefits of delivery must be weighed against the neonatal risks, particularly in environments where administering antenatal corticosteroids at this gestational age is not routine. In the PHOENIX trial (in the United Kingdom), in which delivery was associated with increased neonatal unit admissions but not with increased respiratory morbidity, 60% of women received steroids,[113] whereas in the HYPITAT II trial, in which delivery was associated with increased neonatal respiratory distress syndrome, 1% of women received antenatal steroids.[114] Women who choose to pursue immediate delivery (rather than expectant care) should be reassured that child development and behaviour outcomes are similar at the age of 5 years.[115] A meta-analysis of individual patient data suggested that neonatal risk may not be increased from 36^0 weeks, which is consistent with subgroup analyses in the PHOENIX trial.[113,116]

At term ($\geq 37^0$ weeks), women with preeclampsia should be offered birth, based on the results of the HYPITAT trial.[117] Women who developed gestational hypertension at term in this trial did not benefit from induction, but this subgroup analysis was underpowered. Women with gestational hypertension that developed before 37^0 weeks gestation, or chronic hypertension, may benefit from birth at 38^0 to 39^6 weeks, in terms of reduced incidence of severe hypertension, stillbirth, and cesarean delivery, but the

evidence is observational in nature.[118-120] There is 1 ongoing trial on outcomes (ISRCTN77258279).

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Mode of Delivery

For women with any HDP, vaginal delivery should be considered unless a cesarean delivery is required for obstetrical indications. Vaginal delivery may require early cervical ripening and induction.[121] As women with preeclampsia are at increased risk of postpartum hemorrhage, the third stage of labour should be actively managed.[122] If urgent or emergent delivery is required for maternal and/or fetal indications (Table 3), an emergency cesarean delivery may be indicated. Ergometrine should not be administered to women with any hypertensive disorder of pregnancy, particularly preeclampsia or gestational hypertension; alternative oxytocic drugs should be considered. In centres with access to perinatal pathology, placental pathologic examination may help identify the etiology of preeclampsia.

POSTPARTUM

Immediately Postpartum (Up to 6 Weeks After Delivery)

Following delivery, in women with known hypertension (i.e., chronic hypertension, gestational hypertension, or preeclampsia), BP should be measured at least once daily on days 3–7 postpartum, because of the normal changes in blood pressure over this period. Immediately following delivery, some women with hypertension experience a transient reduction in BP due to the blood loss from delivery, after which, BP normally rises again due to redistribution of extravascular fluid.[24] Other factors (including pain and medications) may further exacerbate this rise, resulting in a peak in BP around days 3–7 after delivery.

Hypertension and preeclampsia can arise for the first time (de novo) postpartum, and postpartum hypertension accounts for up to 25% of all HDPs.[123] Whether hypertension arises antenatally or *de novo* postpartum, BP levels may be significantly higher than before delivery, sometimes in the severe hypertension range (i.e., ≥160/110 mm Hg).[124] Severe hypertension is associated with significant maternal morbidity and mortality, including a higher risk of stroke. Thus, urgent antihypertensive therapy is recommended to reduce BP to <160/110 mm Hg in the short term and, ideally, <140/90 mm Hg, as described earlier in this document.[5]

Given the prevalence of postpartum hypertension and its associated preventable morbidity and mortality, it is important for health care centres to have systems or protocols to monitor, recognize, and treat postpartum hypertension. These systems include inpatient postpartum wards, emergency departments,[125] obstetrical day units, and home care programs.[124] In addition, women with hypertension should be instructed on home self-monitoring of BP, BP targets, and when to seek medical attention; regular BP self-monitoring over the first 2 weeks postpartum may improve long-term BP.[126] Further, health care providers monitoring women following preeclampsia should be alert to their heightened risk of postpartum mental health disorders (e.g., depression, anxiety, and post-traumatic stress disorder) and manage them accordingly.

When considering antihypertensive drugs postpartum, health care providers should be aware that there are limited data on the safety of antihypertensive agents during lactation.[5] In general, antihypertensive agents with low concentrations in breast milk are preferred. There are several open-access, evidence-based sources examining the safety of medications in breastfeeding, including LactMed@NIH (https://www.ncbi.nlm.nih.gov/books/NBK501922/). Oral antihypertensive drugs commonly used postpartum include labetalol, long-acting nifedipine, enalapril, and captopril; all have similar efficacy in lowering BP, although further research is needed to guide clinicians on BP targets and medications.[5,124] Other antihypertensive medications may be considered on an individualized basis.

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After 6 Weeks Postpartum

The majority of women with gestational hypertension and preeclampsia experience normalization of hypertension, clinical symptoms, and abnormalities in laboratory results by 6 weeks to 3 months after delivery.[127] However, normalization of these parameters may take more than 6 to 12 months, depending on the severity of hypertension and proteinuria.[127] For women with persistent postpartum hypertension beyond 6 to 12 months,

investigations for secondary causes of hypertension may be considered (Table 3), and ongoing antihypertensive therapy should be individualized based upon a woman's specific indications for antihypertensive therapy, her cardiovascular risk, and her reproductive plans for future pregnancy.[5]

The 6-week postpartum visit provides an opportunity to counsel women with gestational hypertension and pre-eclampsia on their future obstetrical and cardiovascular health risks.[128]

If not previously discussed, women with a HDP should be advised of their increased risks of recurrent HDP in subsequent pregnancies, although the precise risks estimates are unknown. Women should be educated on evidence-based therapies to lower their risk of HDP in a future pregnancy; these include avoiding weight gain between pregnancies[129] (see also the section on prevention). Referring women to a regional centre can be considered, particularly for those with a history of preterm birth, adverse perinatal outcome, or evidence of maternal vasculopathy on placental pathology.

In addition, women should be counselled on their increased risk of future cardiovascular-related diseases, specifically cardiovascular risk factors (i.e., type 2 diabetes, chronic hypertension, and dyslipidemia), CKD, obesity, cardiovascular diseases (i.e., coronary artery disease, arrhythmias, and heart failure), cerebrovascular diseases (stroke, transient ischemic attack, and dementia), and peripheral arterial disease.[130] The number of women with a previous affected pregnancy, for whom such counselling is indicated, may be twice the estimated prevalence of preeclampsia.[131] Screening and treatment of cardiovascular risk factors should be individualized on the basis of the woman's cardiovascular risk, and health behaviours should be considered as first-line therapy.[132]

CONCLUSION

The HDPs remain an important cause of maternal and perinatal mortality and morbidity, in the short- and long-term. These guidelines update those from 2014, and highlight many areas of high-quality evidence for implementation in clinical care.

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APPENDIX A

Table 1. Key to Grading of Recommendations, Assessment, Development and Evaluation Quality of Evidence

Grade	Definition
Strength of recommendation	
Strong	High level of confidence that the desirable effects outweigh the undesirable effects (strong recommendation for) or the undesirable effects outweigh the desirable effects (strong recommendation against)
Conditional [a]	Desirable effects probably outweigh the undesirable effects (weak recommendation for) or the undesirable effects probably outweigh the desirable effects (weak recommendation against)
Quality of evidence	
High	High level of confidence that the true effect lies close to that of the estimate of the effect
Moderate	Moderate confidence in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Limited confidence in the effect estimate: The true effect may be substantially different from the estimate of the effect
Very low	Very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Do not interpret conditional recommendations to mean weak evidence or uncertainty of the recommendation.

Adapted from GRADE Handbook (2013), Table 5.1.

Table 2. Implications of Strong and Conditional recommendations, by guideline user

Perspective	Strong Recommendation • "We recommend that…" • "We recommend to not…"	Conditional (Weak) Recommendation • "We suggest…" • "We suggest to not…"
Authors	The net desirable effects of a course of action outweigh the effects of the alternative course of action.	It is less clear whether the net desirable consequences of a strategy outweigh the alternative strategy.
Patients	Most individuals in the situation would want the recommended course of action, while only a small proportion would not.	The majority of individuals in the situation would want the suggested course of action, but many would not.
Clinicians	Most individuals should receive the course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that patient choices will vary by individual and that clinicians must help patients arrive at a care decision consistent with the patient's values and preferences.
Policymakers	The recommendation can be adapted as policy in most settings.	The recommendation can serve as a starting point for debate with the involvement of many stakeholders.

Adapted from GRADE Handbook (2013), Table 6.1.